Review Handouts for Medical Pharmacology

Terriann Crisp, Ph.D.

Crisp Enterprises: Pharmacology Instruction and Consultation, LLC

www.pharmprofessor.com

Disulfiram-like Effect When Mixed with ETOT

Drugs that will produce a 'disulfiram-like' reaction when administered with alcohol (ETOH)

Antibiotics

- metronidazole
- Cephalosporins such as cefoperazone, cefamandole and cefotetan

First generation Sulphonylureas

- chlorpropamide
- tolbutamide

Antifungal Agent

- griseofulvin

Major P-450 Inducers and Inhibitors in Pharmacology

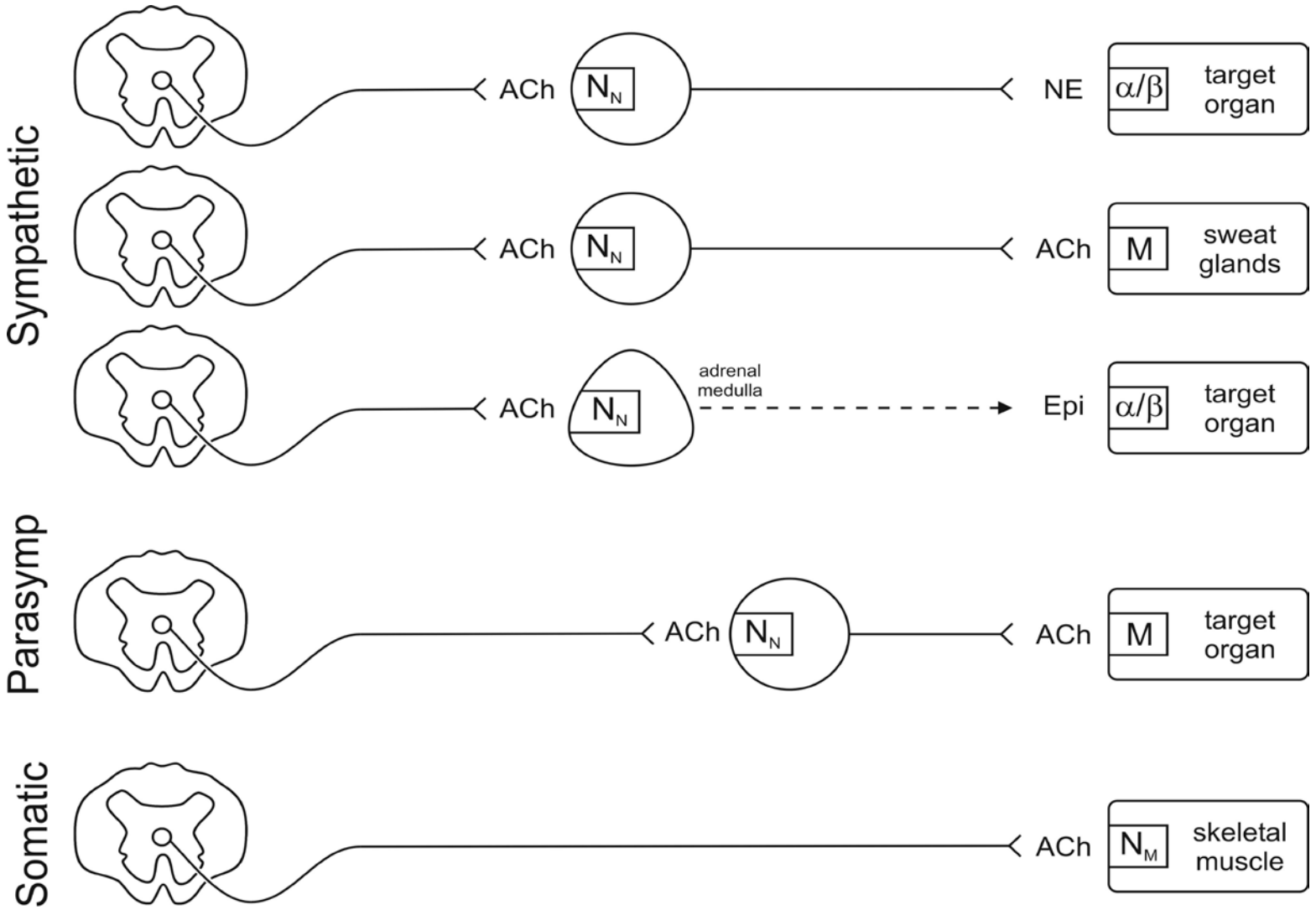
P-450 Inhibitors:

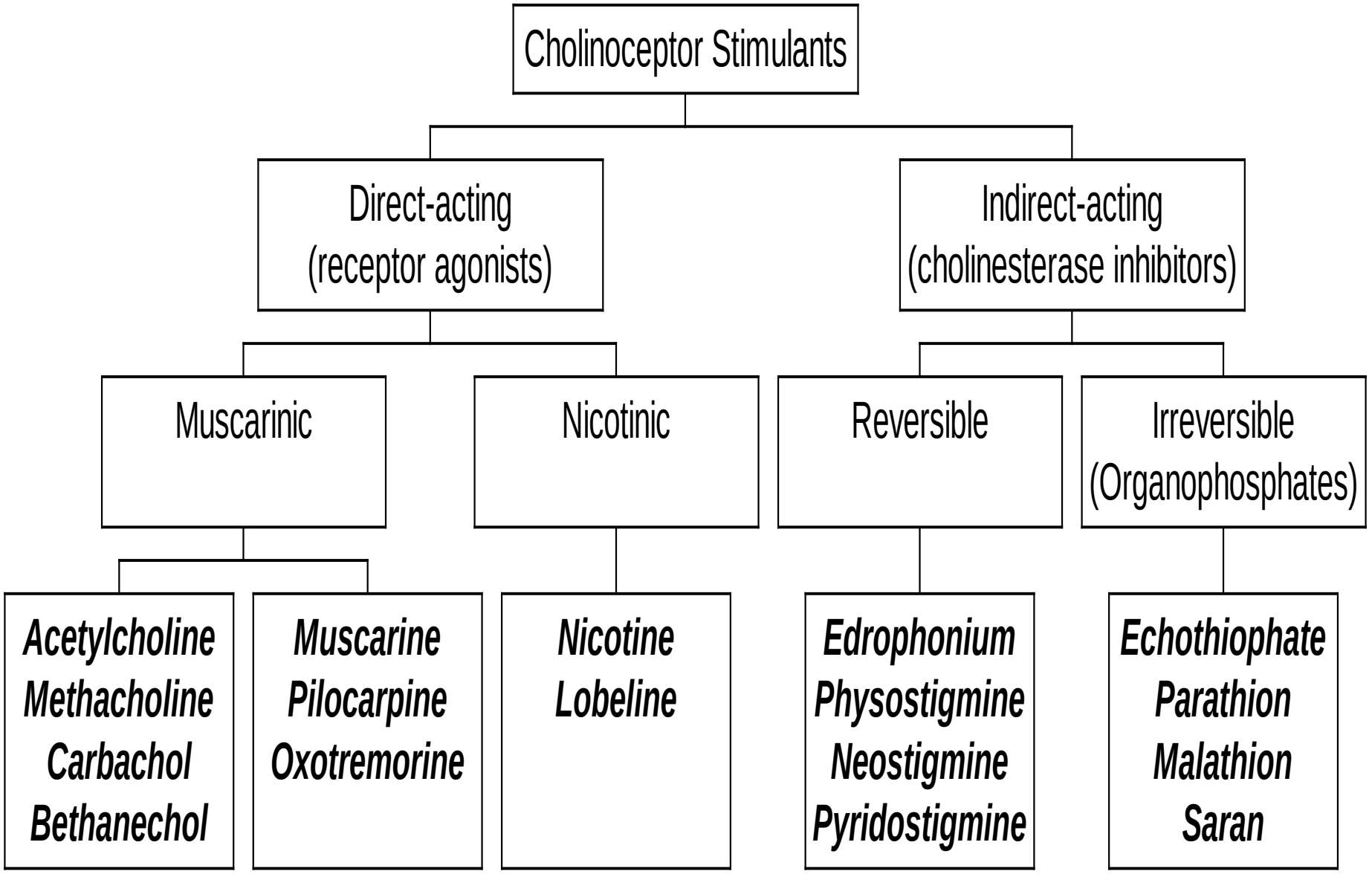
Antiulcer Medication: Cimetidine and omeprazole
Antibiotics: macrolides, chloramphenicol, erythromycin
Antifungals: Ketoconazole and Itraconazole
Acute ETOH
Grapefruit Juice

P-450 Inducers:

Anticonvulsants: Phenytoin, Carbamazepine and Phenobarbital,
Barbiturates
chronic ETOH,
Glucocorticoids
Rifampin
Cigarette smoking

Autonomic Pathways




Cholinoceptor Stimulants
Direct-acting (receptor agonists)
Indirect-acting (cholinesterase inhibitors)
Muscarinic
Nicotinic
Reversible
Irreversible (Organophosphates)
Acetylcholine
Methacholine
Carbachol
Bethanechol
Muscarine
Pilocarpine
Oxotremorine
Nicotine
Lobeline
Edrophonium
Physostigmine
Neostigmine
Pyridostigmine
Echothiophate
Parathion
Malathion
Saran

Review of Muscarinic Agonist and Antagonist Action

Muscarinic Agonist Action	Antimuscarinic Action
Miosis and Accommodation	**dilated pupils (mydriasis) and cycloplegia, photophobia**
Bronchoconstriction	bronchodilation (useful for treating asthma)
Increased GI and urinary activity	decreased GI and urinary bladder activity
Salivation, Sweating	dry mouth, **dry red hot skin**
Lacrimation	**dry eyes**
Defecation	constipation
Negative chronotropic and dromotropic effects in the heart	tachycardia
Few CNS effects	**CNS confusion, delirium, hallucinations** and seizures

SUMMARY OF CHOLINERGIC DRUGS

Directly-Acting Cholinomimetics (muscarinic agonists)

- Acetylcholine
- Methacholine
- Carbachol
- Bethanechol
- Muscarine
- Pilocarpine

Acetylcholineesterase Inhibitors (AChEIs)

- Edrophonium
- Physostigmine
- Neostigmine
- Pyridostigmine
- Parathion
- Soman, Sarin

Muscarinic Blocking Drugs

- Atropine
- Scopolamine
- Ipratropium
- Tropicamide
- Benztropine

Ganglionic Blockers

- Mecamylamine
- Hexamethonium

Depolarizing Blocker

- Succinylcholine

Nondepolarizing Blockers

- Tubocurarine, Gallamine, Pancuronium

Review of Adrenoceptor Agonists

α_1-agonists

phenylephrine
Methoxamine
NE, EPI, DA

α_2-agonists

Clonidine
α-methyldopa
NE, EPI, DA

β_1-agonists

dobutamine
isoproterenol
NE, EPI, DA

β_2-agonists

terbutaline
albuterol
ritodrine
Isoproterenol

Indirect-acting sympathomimetics

Amphetamine – NE releaser
Tyramine – NE releaser
Ephedrine – NE releaser
Cocaine – uptake of DA (CNS) and NE

Review of Adrenoceptor Antagonists and Sympathoplegics

α-adrenoceptor antagonists

- phentolamine (α_1 and α_2 blocker)
- phenoxybenzamine (α_1 and α_2 blocker)
- prazosin, terazosin, doxazosin and tamsulosin (α_1-antagonists)

ß$_1$ and ß$_2$-adrenoceptor antagonists

- Propranolol
- timolol
- nadolol
- pindolol
- labet**a**lol (α_1 and β-blocker)

ß$_1$ "selective" antagonists

- acebutolol
- atenolol
- esmolol
- metoprolol

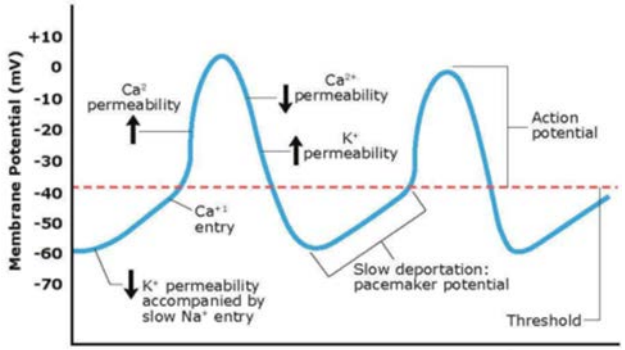
β-Blockers with ISA

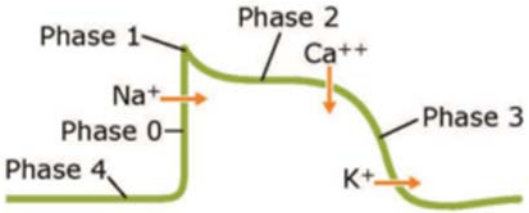
- Pindolol
- Acebutolol

Sympathoplegics

- guanethidine
- reserpine (crosses BBB)

Antiarrhythmic Drugs





Class I (**Na^+ channel blockers**)

Ia – quinidine, procainamide, disopyramide

Ib – lidocaine, phenytoin

Ic – flecainide, encainide – *proarrhythmic*

http://www.nejm.org/doi/full/10.1056/NEJM199103213241201

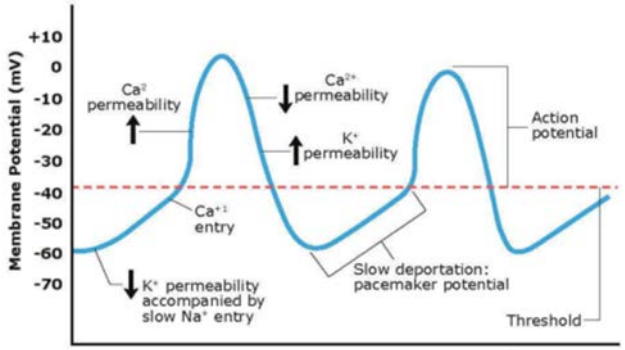
Class II (**β-blockers**) – propranolol, acebutolol

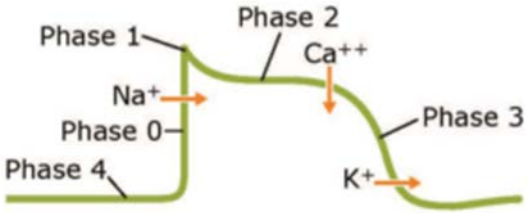
Class III (**K^+ channel blockers**) – amiodarone, sotalol, ibutilide

Class IV (**Ca^{++} channel blockers**) – verapamil, diltiazem

Class V "**Others**" – adenosine, digoxin, atropine

Antiarrhythmic Drugs





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Antihypertensive Agents

Drugs interfering with storage vesicles

Reserpine

Guanethidene

Drugs Altering Sympathetic Activity

α_2 agonists: clonidine and methyldopa

α_1-antagonist: prazosin, doxazosin, terazosin and tamsulosin

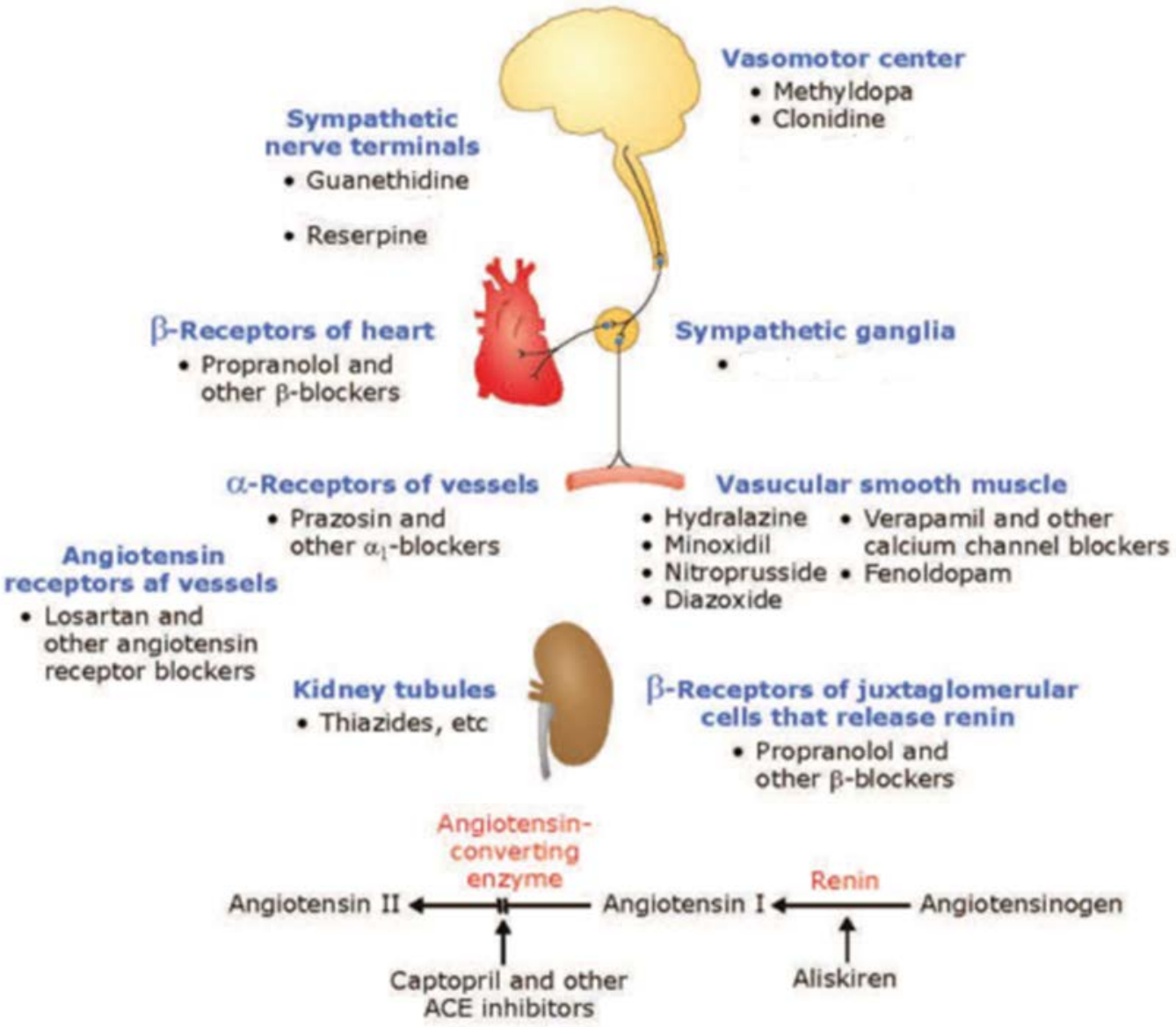
β-blockers: metoprolol, acebutolol, attenolol

Direct-Acting Vasodilators

Hydralazine

Minoxidil

Nitroprusside


Vasomotor center
• Methyldopa
• Clonidine
Sympathetic nerve terminals
• Guanethidine
• Reserpine
β-Receptors of heart
• Propranolol and other β-blockers
Sympathetic ganglia
•
α-Receptors of vessels
• Prazosin and other α1-blockers
Vasucular smooth muscle
• Hydralazine
• Minoxidil
• Nitroprusside
• Diazoxide
• Verapamil and other calcium channel blockers
• Fenoldopam
Angiotensin receptors af vessels
• Losartan and other angiotensin receptor blockers
Kidney tubules
• Thiazides, etc
β-Receptors of juxtaglomerular cells that release renin
• Propranolol and other β-blockers
Angiotensin-converting enzyme
Renin
Angiotensin II
Angiotensin I
Angiotensinogen
Captopril and other ACE inhibitors
Aliskiren

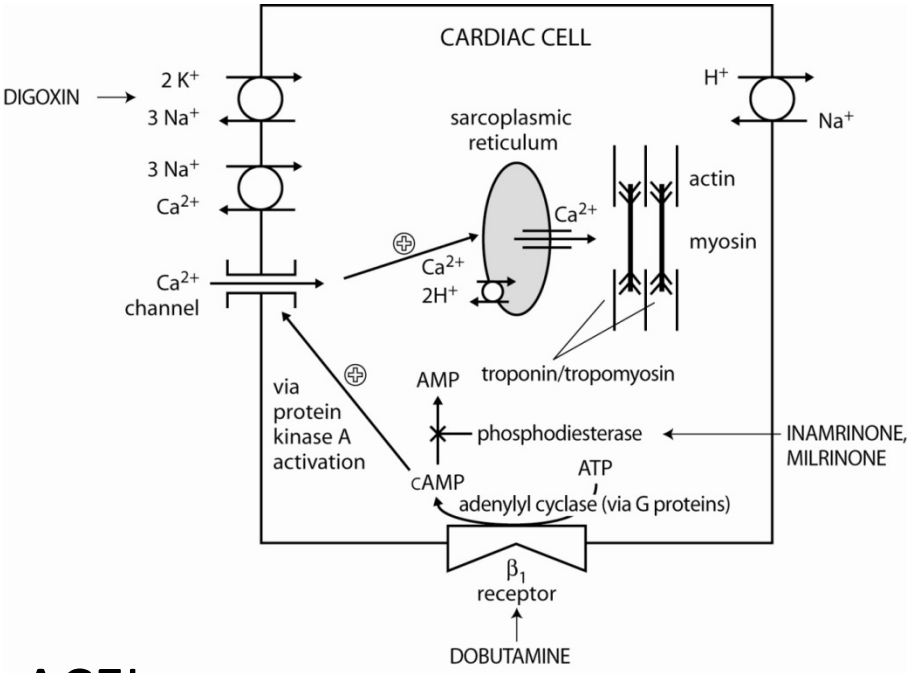
Antihypertensive Agents continued…

ACEIs and ARBs

captopril, enalapril, lisinopril (ACEIs)
losartan and valsartan (ARBs)

Diuretics
Thiazides
loop diuretics

Drugs to Treat Congestive Heart Failure



ACEIs

Captopril:

Enalapril:

Lisinipril:

ARBs

Losartan:

Valsartan:

B-Blocker

Carvedilol:

Diuretic

Spirinolactone

Anti-Anginal Drugs

Nitrovasodilators
Nitroglycerin
Isosorbide

Calcium Ca^{++}Blockers
Verapamil
Diltiazem
Nifedipine - vasospastic angina

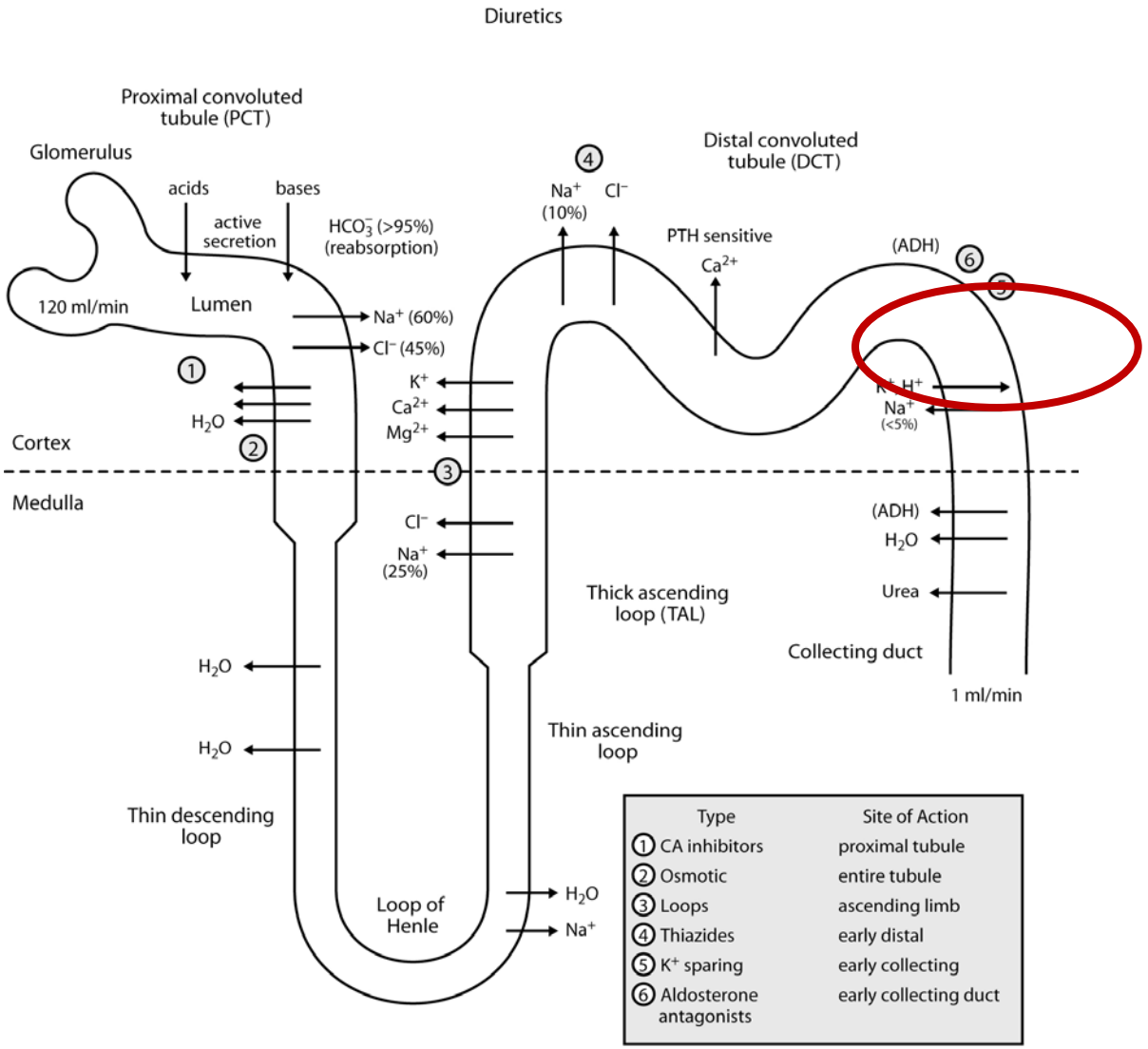
β-Blockers - contraindicated in vasospastic angina
Propranolol
Metoprolol

Use of Antihypertensive Drugs in Comorbid Conditions

Indication	Suitable Drug(s)
HT + Angina	β-blockers, CCBs
HT + Diabetes	ACEIs, ARBs
HT + Heart failure	ACEIs, ARBs
HT + Post-MI	β-blockers
HT+ BPH	α-blockers (tamsulosin or ‘azosin’s)
HT + Dyslipidemias	α-blockers, CCBs, ACEIs/ARBs

Diuretics

See Drugs on Next Page



Actions of Diuretics at the Various Renal Tubular Segments

Diuretic Class	Site of Action	Mechanism
Osmotic Diuretics • Mannitol • Urea	Proximal tubule	Inhibition H_2O reabsorption by osmotic action
Carbonic Anhydrase Inhibitors • Acetazolamide • Dorzolamide	Proximal tubule	Inhibition of $NaHCO_3$ reabsorption (enhances Na^+ excretion)
Loop Diuretics • Furosemide • Ethacrynic acid • Bumetanide	Thick ascending limb of the loop of Henle	Inhibition of active salt transport
Thiazides • Hydrochlorothiazide • Chlorthalidone • Indapamide	Early distal tubule	Inhibition of NaCl reabsorption
Potassium-sparing diuretics • Spironolactone • Amiloride • Triamterene	Late distal tubule and cortical collecting duct	Inhibition of Na^+ reabsorption and K^+ secretion by competitive antagonism of aldosterone (spironolactone) or by direct action (triamterene or amiloride)

Review of Antihyperlipidemic Drugs

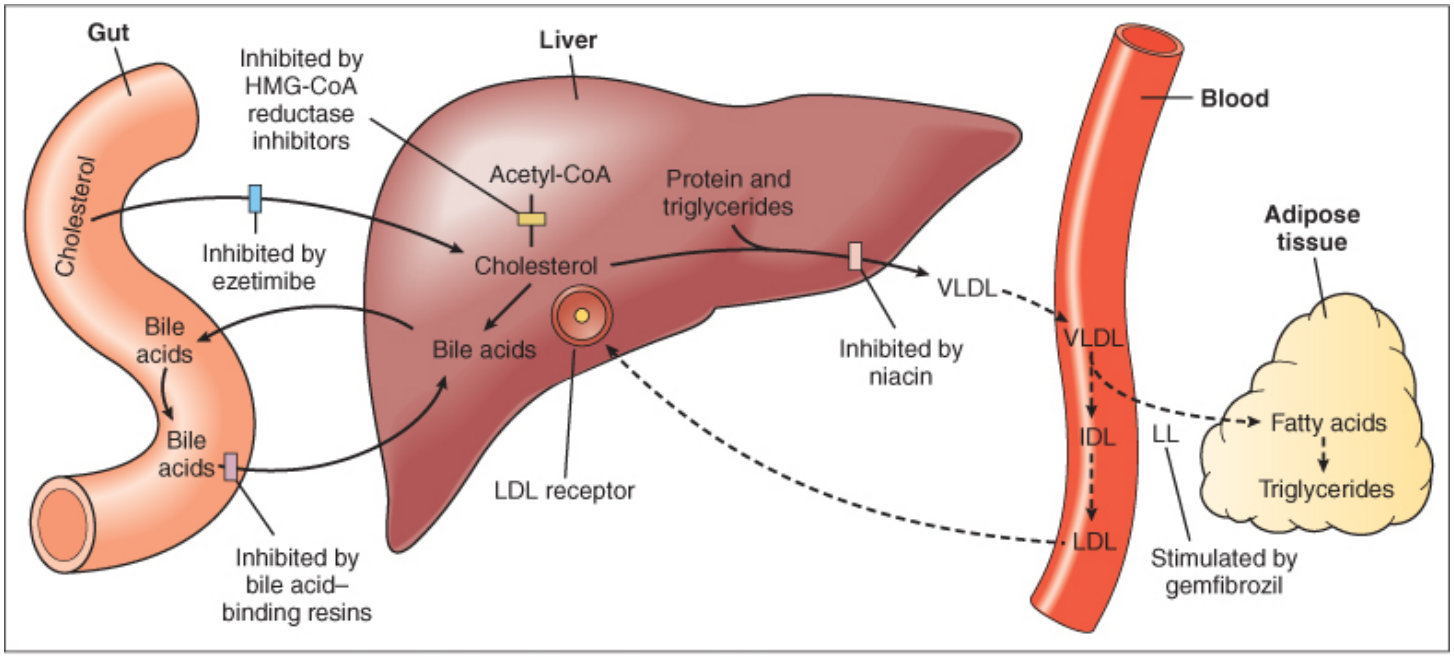
Bile Acid-Binding Resins
- Cholestyramine
- Colestipol

HMG-CoA Reductase Inhibitors
- Atorvastatin
- Lovastatin
- Pravastatin
- Simvastatin

Lipoprotein Lipase Stimulators (Fibrates)
- Gemfibrozil
- Fenofibrate

VLDL Inhibitors
- Niacin - ↓ triglyceride and LDL levels.

Inhibitors of Cholesterol Absorption
- Ezetimibe



Brenner & Stevens: Pharmacology, 3rd Edition.
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TOXICOLOGY OVERVIEW

POISON	ANTIDOTE
Acetaminophen	N-acetylcysteine
Anticholinergics (Antimuscarinics)	Physostigmine
Arsenic and Mercury	Dimercaprol, D-penicillamine
Benzodiazepines	Flumazenil
β-Blockers	Glucagon
Botulism	*Botulinum* antitoxin
Calcium Channel Blockers	Calcium, Glucagon
Cyanide	Amyl nitrite, Thiosulfate
Digitalis Glycosides	Digoxin-specific FAB
Ethylene Glycol	Ethanol, Fomepizole, Pyridoxine
Heparin	Protamine
Iron	Deferoxamine
Lead	**Succimer (DMSA),** EDTA, Dimercaprol
Methanol	Ethanol, Fomepizole,
Methotrexate	Folate, Leucovorin
Opiates	Naloxone, Naltrexone, Nalmefene
Carbamates and Organophosphates	Atropine, Pralidoxime
Serotonin Syndrome	Cyproheptadine
Tricyclic Antidepressants	Sodium Bicarbonate
Warfarin Anticoagulants	Vitamin K

Adopted from Toxicology Secrets (eds., Ling et al.); Hanley & Belfus, Inc. Philadelphia